The Hunterian Oration

ON

HUNTER'S IDEAL AND LISTER'S PRACTICE.

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BY

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ON this day, the 199th anniversary of his birth, we commemorate the services of John Hunter to the science and the art of surgery. In this year we celebrate the centenary of the birth of Lister. Hunter and Lister. From all who have ever served the cause of surgery these two stand apart by reason of the immeasurable gifts which they have conferred upon their fellow-men. May we to-day recall something of Hunter's work and of his ideals in respect of the conquest of disease, which the genius of Lister made possible!

Man's life is warfaro. The individual, the whole race, is beset by foes—unresting, relentless. Against them our defence, if we are ever to subdue them, must be carefully planned, and diligently strengthened. But defence, however stubborn, is not enough. Attacks designed after scientific study of the enemy strongholds and methods, and launched with impassioned zeal, must never for one instant falter. Not all our attacks meet with success. We are cheered when we gain some notable victory, yet when we suffer defeat, as wave after wave of our advance is checked and repulsed, we do not lose heart. Failure inspires us to fresh and still more eager endeavour.

In this year, the centenary of Lister, we rejoice to acclaim the greatest victory ever won by man against his enemies. We who are in active work to-day are perhaps unable to measure the full extent of that victory; for during the long fight, lasting almost exactly sixty years, our standards have been so changed that we cannot truthfully compare our work with that of our intellectual ancestors. Operations from time immemorial so mortal as to be prohibitive are now freely performed without anxiety. Operations formerly unimaginable aro now matters of everyday occurrence. The mere tale of such work done does not adequately illustrate the change. On my last day as surgeon on the full staff of my hospital I performed six abdominal operations. Not one of these was practised by any member of our staff during the year in which I became house-surgeon, nor had such a diagnosis as was made in three of theso cases, and verified at the time of operation, ever then been attempted in the history of medicine. Above all, a statement of facts and a comparison of methods does not in adequato degree convey to our minds the difference of outlook, of the intellectual and spiritual approach of a man to his daily task, as between the surgeon in the days before Lister and since. It is barely possible for us to imagine how men felt about their daily work when an eminent surgeon could speak of his hospital as a "house of death"; when hospitals "were little short of pest-houses," as Lister said;[1] and when the oppressive mortality compelled tho closure of wards or of a whole hospital for months, until the curse was lifted from them.

The change, of incalculable benefit to humanity, is due to one man—Lister.[2] Before Lister's time the surgeon dreaded the almost inevitable consequences of his operation. Lister made surgery so free from risk that we now may say that, with due care in the detailed application of the lessons learnt from him, it is no longer the fatality of the operation itself which is feared. In these days, when a patient dies it is not because the operation leads to septic complications which ho cannot withstand. We fear for him chiefly, if not only, when the extent of the operation is formidable, or when the most sensitive regions of the body, sometimes remote and almost inaccessible, are attacked by methods which half a century ago were beyond the wildest dreams of the most adventurous mind. Our main concern in these days is with the condition of the patient before and after operation. We seek to make him as safe for surgery as surgory has been made safe for him. Lister, in short, has made all the methods applied by the surgeon almost devoid of risk in themselves. The risks run are dependent upon accessory factors—upon the state of the patient, the nature and extent of the disease, the intrinsic susceptibility of organs, or the anatomical conditions responsible for the difficulties which must be surmounted.

Do we fully realize the implication of all these statements? We are at the end of an epoch, indisputably the greatest in our history—the epoch in which manipulations by the surgeon have been robbed of the prohibitive dangers which formerly repelled. Now when failure comes it is tho individual who fails, not the methods of which Lister laid tho eternal and unshakable foundations. Lister by his genius recruited an army of surgeons which has gained astounding victories. The human body from crown to toe has for all time become our indisputable kingdom, within which we may come and go at pleasure, undismayed by the pestilences which menaced us before Lister forever subjugated our enemies. Lister is indeed Captain of the men of Life.

We who inherit the glorious legacy of Lister must not be content merely to enjoy and exploit our incomparable heritage. No great teacher measures his success in contemplation of his own efforts. His greatness lies rather in the work which he inspires others to do—in the tradition not of past accomplishment but of future devotion. Traditions are fostered and increased not by routine observance of ancient ceremony, nor by mute obedience to outworn creed, but by active faith forever seeking new truths and exploring new paths, in conformity with the old spirit and with unchanging devotion to the great ideal of which the tradition is the shrine. There is immortality of the tomb, and immortality of the resurrection. The soul of a great teacher is born again in his pupils. What, then, are we to do with Lister's gift to mankind? We use it already to the immense advantage of the individual sufferer; a therapeutic weapon of unapproached perfection, we are making it, and we must continue, in increasing degree, to make it far moro than that. After the great war the statesmen of Europe, moved by the highest ideals, sought, not perhaps wholly in vain, to convert the allied victory into lasting peace. The statesman's ideal is a warless world. War is to end war. Ideals are not so much for capture as for pursuit, and though the statesman may never attain his ideal, yet the happiness and progress of mankind surely depend upon the grim and perhaps endless struggle to reach it. So, too, for us surgery must be regarded as the most powerful weapon of research upon man and animals ever given to our hands; and the end of research is not the cure only, but, far better, the prevention, of disease.

HUNTER'S IDEAL.

The Oration I have now the honour to deliver was founded 114 years ago as "a lasting mark of respect to the late John Hunter,"[3] Let us turn to Hunter, the greatest surgeon of all the ages before Lister, and see how he regarded the art ho practised. In the opening lecture of each surgical course Hunter said to his students:[4]

> "The last part of surgery, namely operations, is a reflection on the healing art; it is a tacit acknowledgement of the insufficiency of surgery. It is like an armed savage who attempts to get that by force which a civilized man would get by stratagem."

In his *Treatise on the Venereal Disease*,[5] a work more frequently quoted for its glaring errors than for its profound truths, he indicates one of the ways which lead to this ideal, the prevention rather than the cure of disease. He writes:

> "As disease in general should not only be cured but when it is possible prevented, it will not be improper to show, as far as we know, how that may be done: for in this disease we can with more certainty prevent infection, its origin being known." Ho

then adds, "... corrosive sublimate in water, about a grain or two to eight ounces, has been known to prevent the catching of the disease."

Hunter anticipated that a time would come when surgery, gaining much from the general advance of knowledge, might be rendered both knifeless and bloodless. I do not speak with irony when I say that Lister's work has brought us appreciably nearer to Hunter's ideal. It is true that its first effect has been to increase a hundredfold the operations practised, and to cause an advance into territories never before subdued. The advance was timorous, halting, and at first so unsafe that the men who led the thought of the day, whose stubbornness was iniquity, whose changeless idolatry was the worship of the images of their fathers, did not hesitate to demand that he who practised such a deadly operation as ovariotomy should be indicted for manslaughter. Lister so taught us that to-day, with little risk and with incomparable advantage to our patients, we, strong in the faith that our fathers rejected, not only attack disease with remedial operations, we also seek out and expose, we inspect and study it in its deepest recesses, and in its earliest structural manifestations, sometimes discovering its cause, or at least its impressive antecedent, and often tracing the lines of its gradual extension. We are at last coming to appreciate the reaction of living organs upon each other. As I have claimed on earlier occasions, we have created and are slowly building up knowledge from which our predecessors were completely debarred—not new science, but new vision of an old science: the pathology of the living. This branch of surgical learning will continue to grow, and therein surely lies our hope that surgery may one day help to end surgery, by enabling us to discover how those earliest processes of disease may be inhibited. Some claim this as the era of preventive medicine. Is there not preventive surgery also? Hunter was possessed of an ideal. Lister gave the power to realize it. We too wage war to end war. "*Pereant arma bellica.*"

At the end of a long, arduous, and triumphant surgical campaign we, if we are prudent and foresighted, shall survey our equipment and our arsenals and consider the strategy of our next advance. The military leader of to-day seeks help from every branch of science; the victorious leader is he who best knows where to seek the help of which he is in need; who has the genius early and quickly to perceive how all new knowledge can be best applied to the art of war. Surgery too is warfare; its advance is conditioned by contemporary progress in every branch of science, and its virtue lies in the number and the vigour of its allies. Into what alliances, then, has surgery entered with other branches of knowledge?

SURGERY AND THE ANCILLARY SCIENCES.

The science of physics has brought radiology to our aid, and the discovery of the x ray has rendered the living body translucent. After an opaque meal these rays disclose the normal movements of the alimentary canal, and we learn, as in no other way, the functional anatomy of the intestine. Any defect of outline may reveal a structural deformity and perhaps enable us to make a precocious diagnosis of conditions whose terminal stages when neglected are fatal.

The art of the chemist can be allied with that of the physicist, as the work of Graham of St. Louis has shown, with the result that the physiology of the liver, the functional anatomy and the pathological conditions of the gall bladder, the association of gall-bladder activity with movements of the duodenum, may all be studied by a new method. And this method, in alliance with that of the surgeon, realizes another stage in our advance towards the prevention of gall stones, themselves a tardy result of insidious changes originating elsewhere. Chemistry lends its invaluable aid in discovering for us the functional activity of the kidneys, and by its investigation into the cholesterin and calcium content of the blood is helping us to understand some of the problems relating to the functional activity of the liver and gall bladder. Such conditions as acidosis and alkalosis offer impenetrable secrets if chemistry is not brought to our aid.

Physiology by its inclusion in the Faculty of Medicine acquires a double function: it remains a pure science, directing its inquiries solely to the advance and perfection of knowledge; but it becomes also an applied science, in league with clinical medicine and surgery. As he sees his conquest of knowledge applied practically to the saving of human life the physiologist will be encouraged to yet closer study of normal and aberrant vital processes in man. He too should stand with the surgeon by the bedside. The great gap between the powers of the surgeon and the aid which the physiologist might give would thereby be reduced, and the reproach removed from his science that in this sense it is lagging far behind. The surgeon's activities enable him to uncover the hidden mysteries of early structural changes. He offers new opportunities for the study of normal and perverted function to the physiologist, with whom he might inquire into those early functional changes which correspond to and are caused by organic disorder. The surgeon seeks earnestly to know what degree of impairment of function is to be attributed to the textural changes which our new methods have revealed to us. The physiologist may tell us much that we are eager to learn of the effects of our manipulations upon the normal activity of tissues, and of the full or imperfect return of function when diseased tissues have been removed. With his help we may learn what without him we may never learn—the significance and the methods of the causation of early symptoms, and the origins of those pathological changes with whose late mutilations we are, unhappily, only too familiar. With our help he has learnt what otherwise he could not learn—that, for example, the spleen by an excessive destruction of red cells may be responsible for a condition of jaundice, and that the removal of the enlarged spleen results in the disappearance of the jaundice, which is thereby demonstrated to be of haemolytic origin. Physiologist and surgeon are, far more often than is realized, necessary to each other, and a closer communion should exist between them. Many of the truths the physiologist endeavours to teach can be demonstrated more clearly in the wards than in the laboratory, and are therefore, because of this human interest, impressed almost indelibly upon the minds of students. The phenomena of cerebral compression, of Traube-Hering curves, of Cheyne-Stokes respiration; the symptoms of hyperthyroidism, and those produced when the secretion of the thyroid gland is diminished or absent; many of the aspects of jaundice, in addition to the demonstration of haemolysis as its occasional cause, and of the relations between the liver, the spleen, and the bone-marrow; illustrations of the normal and aberrant functions of the kidney; changes in the chemistry and constitution of the blood, may all profitably be discussed in the ward rather than in the laboratory or the lecture theatre. Students would then realize from their earliest days the truth which later comes almost with a shock—that physiology and anatomy are not fundamental subjects, but are interstitial, and should grow alongside and be incorporated with the facts of clinical medicine and surgery, which they illuminate and explain.

Interstitial tissue has as one of its functions the carrying of blood vessels to nourish cells whose activity is dependent upon the richness of their blood supply. Biology provides the interstitial tissue of surgery; the activity and the growth of surgery depend upon the nourishment which biology may bring. Unless surgery calls in the aid of all the sciences with which biology is related it will remain as static as ancient geometry, whose figures were drawn once for all. Modern geometry is concerned with function, with the variations of movement by which a figure is described. Surgery's concern in the future will not only be with the states produced—with established organic disease—but with its allies it will help to eradicate some of those variations in function by which perhaps they have been caused, with which they are associated, and by which their presence is declared.

If sometimes we blame Sharpey and his school for the unhappy cleavage between anatomy and physiology[6] we must at least acknowledge the great debt we owe to him for laying so firm the foundation of new methods for the

studying of functional anatomy in man and in animals. Physiology, with its offspring biochemistry, has introduced physical and physico-chemical methods—methods of quantitative observation which have supplemented where they have not supplanted the merely qualitative methods. The brilliant work of Sherrington, Lucas, and others upon the nervous system gave us fresh conceptions of it; further advances along their lines were becoming difficult until the application of thermionic valves made it possible, by recording the transmission of impulses in the afferent nerves, to investigate the effects of stimuli upon the sensory end-organs. And in the interpretation of symptoms, a study to which my old friend James Mackenzie bent the strength of a most eager and original mind, physiology alone can read the occult significance. In acute pancreatitis there is, as Halsted,[7] a great benefactor of mankind, first told us, a lividity of the face. Why? Is it due to some disordered action of the respiratory system imposed by the closeness of the affected organ to the diaphragm and the structures which lie above it, or is there circulatory stasis, or alteration in the blood pigment?

Physiology is the master of all the methods by which these three possible causes may be quantitatively investigated. Estimations of the oxygen saturation of the arterial blood give information of disturbance of respiratory function—information which we may compare to that derived from a measurement of the amount of blood urea when the renal functions are deficient. Estimations of the carbon dioxide combining power of the blood are essential if we are to recognize the presence and the degree of acidosis. Circulatory stasis may be gauged by the ethyl iodide method of measuring the circulation rate. Alterations of the blood pigment are detected by the spectroscope, and quantitative estimations of abnormal pigments are readily made after the method of Hartridge.

Like the physiologist, the bacteriologist is engaged in work which is ranged alongside our own. The more he discovers of the offensive powers of bacteria and of the defensive mechanism of living flesh under their attack the nearer are we brought to our surgical ideal. The alliance between bacteriologist and surgeon has been necessary for the proof that the true estimate of an antiseptic is not measured only by its bactericidal value tested in the laboratory, but also by its power to encourage the blood serum or the tissues themselves to ward off and to break up an attack. Hunter, with the crude methods which were all he had at his disposal, demonstrated the tryptic power of wound discharges, and anticipated a part of the admirable work of Almroth Wright during the war. Who could have imagined, when Lister's work began, that to-day we should be able to keep tissues alive in our laboratories, breeding them and growing them in captivity, separating the one kind from the other, noting the influence which one type of cell is able to produce on its neighbours, and thus coming by the kind of knowledge which John Hunter so earnestly sought—a knowledge of the intrinsic processes of growth and repair? The problem of malignancy is now installed in our laboratories, and the cancer cell is being compelled to yield most reluctantly some of the complex secrets of its Bolshevist behaviour.

The old art of vital staining, which Hunter learnt from Belchier of Guy's, has taken on new improvements: by means of suitable dyes we can now select special elements in the living body, trace their movements, and note their conduct. The experimental embryologist, too, can help us if we seek to know in what manner the various tissues of the body come into existence.

Hunter: Pasteur: Lister.

These, then, are the allies of surgery in the great war: Biology in all its branches, Chemistry, Physics, Radiology. Never before has the master surgeon had such bountiful resources at his disposal. He cannot afford to neglect a single one of them. The urgent problem of our time, therefore, is a dual one: We must seek to determine the line of advance which surgery will trace in the years ahead, increasing and strengthening our alliances; and we must earnestly discover how the leaders of our army of advance are to be trained. Are the old methods, which in their day served so well, still enough; or is the form of warfare already so changed, and now so rapidly changing, that a new discipline and a wider knowledge are needed?

To answer these questions we must look backwards, and, calling upon our past experience, seek in the records of our great masters not so much what their knowledge was, but what methods they pursued as they qualified themselves for great leadership. We shall find at once that Hunter and Lister, incomparable among surgeons, each put himself through a long and arduous training, never resting in his inquiries as to the activities of living matter, as to its behaviour in health, and its reactions in disease. At the threshold of our survey we recognize that the activities of our two leaders are not unrelated. Hunter's professional life covered the latter half of the eighteenth century, Lister's the corresponding half of the nineteenth century; between them there intervened two generations of surgeons. My distinguished predecessor, the late Sir Rickman Godlee, who gave this oration in 1913, tells us in the Life of his uncle, Lord Lister,[8] that "Hunter was Lister's greatest hero"; that "his copy of Palmer's Life of Hunter was marked in many places by pencil notes which show that he was studying it at least as early as 1855"; that "a proof of Sharp's engraving of the portrait of Hunter by Reynolds, which had belonged to Syme, hung in his study"; that "he always spoke of Hunter with reverence." Further, if we turn to the paper[9] which Lister read to the Medico-Chirurgical Society of Edinburgh in March, 1858, on the "Causes of the coagulation of the blood," we find evidence of his early admiration of Hunter.

> "The nearest approach," he wrote, "which I have been able to find to such an observation [that blood which is retained in the smaller veins of the body remains uncoagulated] is contained in that inexhaustible treasury of original observations and profound reflection, the works of John Hunter."

If I may borrow a simile from the football field to express the relation of these two great men, I would say that it was Pasteur who made the final pass to Lister possible; it was Hunter's captaincy in the scrum that placed Lister in the scoring position. Indeed, we have to admit that while Hunter's resource in midfield has never been excelled, or even approached, and though the ingenuity with which he worked the surgical ball towards the goal remains unsurpassed, yet when he was in a scoring position and we were counting so confidently upon a "try," the ball was fumbled, and our hopes were foiled. The young surgeon of to-day can learn almost as much from Hunter's mistakes as from his triumphs.

Hunter's Discipline and Methods.

Let us now examine the discipline to which John Hunter submitted himself to attain his leadership. He is the "Dick Whittington" of British surgery. In September, 1748, at the age of 20, he left his home, an upland farm in the parish of Kilbride, eight miles to the south of Glasgow, and, travelling on horseback, he entered London in a little under a fortnight, alighting in Covent Garden, where his brother William kept a school of anatomy. William Hunter was beyond doubt the foremost medical teacher of his time; his best pupils caught from him the spirit of research: among his inspired disciples were John Hunter, William Hewson, William Cruickshank, Charles White of Manchester, and William Hey of Leeds, the founder of the Leeds Infirmary, the first stone of which was laid in 1767 by Edwin Lascelles, the first Lord Harewood. In 1751, after three years of study, John Hunter counted himself a qualified surgeon; he remained in his brother's school to teach and to research, at what salary we cannot now tell, but assuredly it was a small one. John Hunter thus entered the critical years of his life, for the career of a young surgeon was determined then, just as it is to-day, not so much by his conduct during the years of pupilage, as by the use made of the period after qualification. The problems which a young surgeon first attacks, and the methods he employs to solve them, are suggested to him by the age in which he lives and by the school in which he has been trained. In John Hunter's youth a knowledge of the human body was being extended

by a skilled use of the art of injection. And so we find him in his earlier years following arteries to their ultimate termination, tracing the course of lymphatic vessels, unravelling the structure of the testis and kidney by means of an expert use of the injecting syringe and of the hand lens. He remained in his brother's school teaching and researching until the spring of 1761, when he entered his thirty-fourth year.

Here is a list of the subjects he investigated during that period. He began to note the earliest stages in the development of the chick[10] and continued this study to the end of his life, deriving from it guidance for the interpretation of the phenomena of repair and of disease. We find him exposing the thoracic viscera, using artificial respiration, and noting accurately what happened to heart and lungs when the air supply was withdrawn and when it was renewed.[11] He studied respiration in birds, keeping cocks alive which breathed through the cannulae inserted in their air sacs instead of through their windpipes.[12] He carried out a series of experiments on absorption from the bowel in various animals; the experiments were well planned and skilfully executed, but he drew from them a wrong inference—one which misled him subsequently time after time—in the interpretation of the processes of disease. He believed that these experiments proved that all the products of digestion were absorbed by the lacteal or lymphatic system, and that none entered by the veins.[13] Our hero, as we have seen, was often weak when he approached the goal posts. We find him tracing out the distribution of nerves in the nose and giving, for the first time, the right explanation of why the fifth pair of cranial nerves should enter into the field of mucous membrane supplied by the olfactory nerves.[14] The description he then gave of the descent of the testis[15] and of the vital phenomena which attend that still mysterious operation has never been surpassed. He kept a tame kite to prove that a stomach accustomed to a flesh diet could be educated to deal with one which was purely vegetarian; he noted the phenomena of digestion in the stomachs of fish, fowls, dogs; he explained *post-mortem* destruction of the stomach.[16] He placed pieces of raw meat in suppurating wounds and observed the digestive effects which followed; he measured the digestive (or tryptic) action of pus.[17] We find him deeply interested in the formation of pus upon the unbroken surfaces of serous and of mucous membranes. He began a series of observations on the uses of the vesiculae seminales,[18] and was led thereby to investigate experimentally the potent and mysterious influence which testis and ovary exercise on the development and growth of the body.[19] We find him seeking signs to distinguish between tissues in which life was latent and those from which life had already vanished. He believed he had discovered the organ of hearing in fishes, and sought to discover an explanation of the curious fact that the ovaries of eels were always destitute of ova.

As a collector—like Pascal a *ramasseur de coquilles*, who often found a pearl of great price—as an observer of incredible industry, gathering facts just for the sake of their individual value and without at the moment any care for their relative significance or for the effect of their impact upon other facts, he ranks second only to Hippocrates. But when these facts were stored in his mind and illustrated by a series of specimens he was by no means inexpert in their interpretation or in raising a general truth from a multitude of singular examples. But as we read we seem to be oppressed by the verbal difficulties he encountered. The words will not come. Even the constructive thoughts may sometimes appear to be absent, puny, or unmanageable. He cannot get his mind round them. If by chance we seem to think that he has done so, the splendour of his thought is disfigured by his uncouth language. Abernethy is not alone in telling us of Hunter's paucity of language and of his inaptitude in its use; but we need no other evidence than that which his own works rarely fail to give us. His letters are the same. Illiteracy is not absent from them, though their meaning is often clear enough, especially when express instructions are given. It is when Hunter endeavours to rise to abstract generalizations that we see this incapacity chiefly and lamentably displayed. Obscurity of language, I believe, even in abstract matters, often means obscurity of thought. Words may come after thought, but not long after, surely. Hunter's defects in language were due in part, no doubt, to the absence of any early education of value, but they were not lessened by his studious avoidance of the work of others. His rebuke to Jesse Foot, as brutal and irrelevant as many of Johnson's, would have confounded anybody, but it is irrelevant nevertheless, and it was a confession of his own imperfection.

After spending fully twelve years experimenting, John Hunter in the spring of 1761, and in the thirty-fourth year of his age, engaged in the practical work of his profession and was appointed surgeon to the army. In the summer of 1763 he returned to London on half-pay and commenced practice. He bought "a piece of ground called Earl's Court, near the village of Brompton, and two miles from Hyde Park Corner," on which he built a small house. Earl's Court, his week-end cottage, was soon converted into a zoological garden and experimental laboratory; many new problems engaged his mind and several avenues of investigation were opened up there; all of them were made to converge on the same subject—the behaviour of living matter under all conditions. It was not until 1768, when he was 40 years of age, that his private practice began to grow, enabling him to take a lease of the house, 42, Jermyn Street, vacated by his brother William. We may now consider him, after an apprenticeship of twenty years, fairly launched in practice. Three years later he considered that his income justified him in undertaking the responsibilities of marriage.

We see, then, this leader of surgery of the eighteenth century devoting twenty years of his life to arduous observation and experiment so as to qualify himself for the practice of his art. There has probably never been a man in our profession with so wide an intellectual interest, so profound a knowledge of so many varied subjects wholly derived from direct personal inquiry and observation. His industry was inexhaustible. He had no equal either as physiologist or pathologist; he was already first among comparative anatomists, and was indeed one of the founders of this science. He was a naturalist, all subjects in animal and vegetable physiology seeming to attract him. All his unequalled attainments as biologist were brought to the service of surgery, in his hospital work and finally in the largest private practice of his day. Before Hunter's time surgery was a thing apart, independent of all other sciences, ostentatiously aloof from them, and governed only by the experiences and aptitude gained in the day-to-day practice of the art. All advance was therefore slow, even when recognizable, and was largely empirical. No physiological knowledge, nor any experimental discovery, broadened the old path or opened up new ones. Hunter changed all this. Not the least of his achievements was that he made alliances for surgery, and linked it inseparably with biology. Hardly a day passed without some experiment. I may quote a statement of his to show how he regarded experiment.[20]

> "In pursuing any subject, most things come to light by accident; that is, many things arise out of an investigation that were not at first conceived, and even misfortune in experiment has brought things to our knowledge that were not, and probably could not, have been conceived; on the other hand, I have often devised experiments by the fire-side or in my carriage, and have also conceived the result; but when I tried the experiment the result was different, or I found that the experiment could not be attended with all the circumstances that were suggested."

This statement helps in some degree to explain the number of apparently unrelated subjects which Hunter explored in his younger years. As he opened a new subject, he still continued to investigate the old; at the time of his death he had over fifty portfolios in use, each relating to a particular line of investigation.

The "misfortune in experiment" has its counterpart in operative surgery. An interesting little paper might be written on "The advantage of error in medicine." We may recall Spencer Wells's operation for an "ovarian cyst," when tuberculous ascites was found and the surgical treatment of peritoneal tuberculosis inaugurated. The

same distinguished surgeon, a pupil of the Leeds school, operating upon a jaundiced girl of 18 for "fibroid tumour of the uterus," discovered that the tumour was not pelvic but splenic. He removed the spleen: in a few days the lifelong jaundice was gone, and the surgical treatment of haemolytic jaundice was begun. So McGill, the pioneer in the operation of prostatectomy—precedence in which is so foolishly claimed for others—removed what he believed to be a "tumour at the base of the bladder." When I, acting as his house-surgeon, examined the tumour microscopically and found that it was prostatic, I felt that I had the chance to twit my beloved chief with his error. His reply when I told him of his mistaken diagnosis was, "Then why don't we always take the prostate out when it projects into the bladder?"

Lister's Discipline and Methods.

When we compare Lister's preparation for professional leadership with that of John Hunter we are impressed rather by the resemblance than by contrast. Lister, the greatest material benefactor of mankind that the world has ever known, began his medical studies at University College, London, at the age of 21, in 1848, exactly a century after John Hunter had settled down to his work in Covent Garden. In the hundred years that had passed medical education in London had undergone a revolution; voluntary schools had almost disappeared, to be replaced by the organized schools and colleges with which we are familiar to-day. John Hunter was Scotch, Lister English, his ancestry coming from Yorkshire and Cumberland. John Hunter owed much to his brother, Lister still more to his father, who was not only a successful man of business, but also a Fellow of the Royal Society. William Hunter, who impregnated the mind of his brother, drew his own inspiration and owed his intellectual guidance to the Monro-Cullen school of Edinburgh. Lister was early influenced by William Sharpey and by Wharton Jones, both Edinburgh men steeped in the traditions of this very school. After qualifying in 1851, and taking the Fellowship of this College at the age of 25, Lister's first research was begun: it was concerned with the contractile tissue of the iris.[21] The injection syringe, the new instrument which had served Hunter so well, had been displaced during Lister's youth by the microscope. We rejoice, nevertheless, to notice that when Lister applied this new instrument to the tissue of the iris, it was the function rather than the form of this structure which excited his interest. In this investigation, and in another[22] begun in 1852, "Observations on the muscular tissue of the skin," we recognize that, influenced by William Sharpey, he had become familiar with discoveries made in other countries, notably with those of Kölliker in Germany. But clinical work was not forgotten, and a house-surgeoncy at University College was followed by perhaps the most critical event of Lister's life. In tracing the motives which have directed the progress of medicine we are constantly reminded of the influence and the power of great teachers. Such men are gratefully remembered by posterity—not so much for the work which their own hands or minds have created or have modified; not for their written words which so soon seem to possess little more than an antiquarian interest; not for their spoken words, which, though at the moment of their delivery they may walk up and down in the hearts of men and stir them to new thought or to great action, yet seem so frail and cold and lifeless when the morning comes—not for any of these, but for the spiritual legacy they bequeath to those trained in their own methods and inspired by their own zeal. It is this which gives posthumous life—the true immortality.

Not the least of the claims that John Hunter makes upon our reverence is that he was the first founder of a School of Surgery. He was not distinguished as teacher. "He had not the happy talent of displaying the stores of his mind, nor of communicating to others the same perception of the importance of his facts and opinions as he himself entertained."[23] Abernethy said his language was "inelegant and often coarse"; "his delivery heavy and unengaging"; "his method confused with attempts to find words for thoughts, or else to read from little scraps of paper." Yet despite these unattractive or even repellent qualities, men who themselves influenced surgery for generations afterwards, whose influence still survives—Abernethy, Astley Cooper, Cline, Everard Home, Blizard—all boasted of being his pupils, and taught his method until it became, and still remains, a tradition in their schools, and from them has spread to every school of medicine in the world, where Hunter is recognized, unchallenged, as the founder of scientific surgery. So, too, our debt to Italy will be forever unrequited while we remember that it was the magnetism of Fabricius that drew Harvey to Padua. But for Fabricius and the magic of his work the discovery of Harvey, the great glory of British medicine, might not have been made for generations.

William Sharpey, whose lectures "inspired me with a love of physiology that has never left me," had not only Lister's future, but also all that this meant for mankind, in his own hands when he sent Lister to Edinburgh to the "safest surgeon" of his day, James Syme. It was an almost incredible exodus. When the Hunters came southwards they followed a national habit established for centuries, and never permitted to fall into disuse—a habit which incited the characteristic irony of Samuel Johnson. When Lister went northward he founded a new tradition and made a novel breach in a custom which seemed to have become as firmly accepted as a law of nature. Lister's most distinguished successor in his chair of clinical surgery, my old friend Harold Stiles, made the same adventure, to Scotland's great advantage.

London hardly notes and seems but little disturbed by the arrival and the progress in her midst of young medical men from Scotland. (Whatever would she do without them?) Edinburgh, one may suspect, raised her eyebrows when she saw a young doctor from London established as Syme's house-surgeon; and she must have rubbed her incredulous eyes when, within two years, she saw him become an extramural lecturer in surgery within her own stronghold. It is quite impossible to exaggerate the importance of this teaching appointment on Lister's future. He met his students—the ultimate number in his first class was seven—on Wednesday, November 7th, 1855. Lister believed, as Hunter had believed, that the beginning of surgery was a knowledge of the process of inflammation; and accordingly he had resolved, before his lectures commenced, to obtain a new first-hand acquaintance with inflammatory processes as watched in living tissues. Clearly he realized long before the humblest of his intellectual descendants the need to study the "pathology of the living." A frog was caught in Duddington Loch—surely the greatest frog in history, honoured by being made the subject of this research. Why did not someone suggest to Lister when he was granted arms that this frog should be immortalized in heraldic device? The web of this frog's foot gave all the necessary opportunities for the inquiry. Lister had many new advantages over Hunter: he knew that the tissue he examined was made up of living units—cells; he had at his disposal a powerful microscope, which could mark the behaviour of these cells; and Claude Bernard in 1853 had taught him the existence of vasomotor nerves. It was during the examination of the frog's web that Lister made a biological discovery of the highest importance—one which experimental biologists are still exploiting: that pigment-containing cells such as are seen in the frog's web give more easily visible, and more delicate, reactions than any other kind of living cell, when subjected to a physiological or a pathological stimulus. This quality enabled him to study the effects of inflammation in terms of individual cells. He was able to prove that these pigment cells still gave vital responses fifteen days after the leg had been amputated.

The list of researches carried out by Lister between the time of his arrival in Edinburgh in 1853 and his appointment to the chair of surgery in Glasgow in 1860 would almost suggest that he was seeking to fit himself to become an experimental physiologist or pathologist rather than surgeon. I would earnestly emphasize this point, for its significance in Lister's day was far less than it is to-day, when the full harvest of his work is ready to be gathered. In most of these researches we can clearly see the strong

influence of John Hunter. It is not accident, surely, that the men who have done most for surgery trained themselves rather as research workers than as practitioners, that they revelled in and set out to master one problem after another in biology. Lister's acknowledgement of the immense influence of Hunter upon him is not in the least overstrained. If the spirit of Hunter watches over his Museum and this College, as we hope it may, how infinite must be its pride in the thought that the one man greater in service than Hunter himself was his direct intellectual offspring!

Let me recall the names of a few of Lister's early papers: that "On the flow of the lacteal fluid in the mesentery of the mouse,"[24] begun in 1853 and published in 1857, is a direct extension of Hunter's experiments on absorption;[25] the communication on "The persistent vitality of the tissues"[26] is founded upon observation made by Hunter himself on the same subject. The studies on "Coagulation of the blood" began by observing what happened in the veins of "sheep's trotters" taken from the shambles. By devising new and critical experiments he was able to carry the knowledge concerning coagulation to a point far beyond that which Hunter had reached a century before him. Yet his methods were clearly modifications of Hunter's. Lister's vocabulary, indeed, was still that of Hunter: for he spoke of the "solids" of the body, of "preternatural stimuli," of the "disposition of the tissues," of "inherent tendencies," and of "sympathetic irritation."

The Antiseptic System: Preventive and Curative.

The events which followed Lister's arrival in Glasgow are too well known to all the world to need more than the briefest recapitulation. Lister was then 33 years of age, almost the same age as Hunter when he joined the army as a surgeon. As a result of seven years of a preparatory experimental investigation, conjoined with a wide clinical observation which was closely related to it, he had become immersed in all the problems relating to inflammation and suppuration. He had already formulated a hypothesis that suppuration was due to putrefaction, and in 1865 was ready to put his supposition to a practical test. Pasteur's epochal discovery that putrefaction was due to "germs" set matters going. Lister wrote:[27]

"To prevent the occurrence of suppuration, with all its attendant risks, was an object manifestly desirable; but till lately apparently unattainable, since it seemed hopeless to attempt to exclude the oxygen, which was universally regarded as the agent by which putrefaction was effected. But when it had been shown by the researches of Pasteur that the septic property of the atmosphere depended, not on the oxygen or any gaseous constituent, but on minute organisms suspended in it, which owed their energy to their vitality, it occurred to me that decomposition in the injured part might be avoided without excluding the air, by applying as a dressing some material capable of destroying the life of the floating particles."

Lister was first of all concerned with the destruction of organisms after they had obtained access to wounds. He knew of the experiments with the Carlisle sewage, and of the bactericidal properties of carbolic acid. He observed carefully the effects produced upon living tissues by antiseptics, and concluded that the reparative processes in a wound were not thereby weakened. We are apt, however, to forget the gradual change that came over Lister's views, and the effect this had upon his practice: how he came to a full realization of the essential powers of defence possessed by the living tissues, and of our obligation to protect and if possible to increase them. Sir Rickman Godlee, who knew more of Lister than any man, has written that Lister before 1881, when he first told the world of his changed opinions, "had long recognized and taught that healthy living tissues exercised an inhibiting influence on the growth of micro-organisms. . . . He therefore began to wonder, whether if only slightly damaged, for example, by the incision made by a very sharp knife, the living tissues of any wound might not be able to deal with a certain number of germs by their own efforts." This we gleefully observe is a return to Hunter's work in which he recognized the "powers," "disposition," and "action" of living tissues. It may not be inappropriate to quote Lister's own words. He writes:[28 29]

"The original idea of the antiseptic system was the exclusion of all microbes from wounds." Again, "During the operation, to avoid the introduction into the wound of material capable of inducing septic changes in it, and secondly to dress the wound in such manner as to prevent the subsequent entrance of septic mischief." Again, "In wounds already septic attempts are made with more or less success to restore the aseptic state." Again, "In speaking of the antiseptic system of treatment I refer to the systematic employment of some antiseptic substance so as entirely to prevent the occurrence of putrefaction in the part concerned, as distinguished from the mere use of such an agent as a dressing"; and further, "I always endeavour to avoid the direct action of the antiseptic substance upon all tissues."

The distinction between the preventive and the curative use of antiseptics is in many respects that existing between, on the one hand, the power of a germicide as determined by experiments *in vitro*, and, on the other hand, its capacity to destroy organisms when it is introduced among the living and the dead tissues of a wound. In the former there is a direct conflict, a clean fight between the microbe and the chemical agent. Few or none of the many intervening conditions are present which have to be considered when a bactericide is introduced into a wound cavity wherein there are multitudes of actions and reactions which even now seem very obscure and are so often conflicting.

We may therefore regard Hunter and Lister as bridge-builders; it is out of a multitude of scientific observations, of apposite inferences, and of wide generalizations that such bridges are built, stone by stone, arch by arch. Posterity will perhaps remember only the one bridge—permanent, indestructible, all-sufficing—of Lister. Across that bridge we have swarmed, a triumphant host, and a vast new territory has met our almost incredulous eyes. Hunter was forever building bridges, ambitious in design, firm in their foundations, but always left unfinished. Some day new architects will come and give them the full span which Hunter surely meant them to have. It is remarkable to note how often he anticipated the lines along which we see that modern surgery is making its advance. Cultures of both benign and malignant tissues are now being kept alive by methods which, devised by Dr. Ross G. Harrison while studying the growth of fibres from the nerve cells of a tadpole, have been rapidly developed by Alexis Carrel. John Hunter, too, tried his hand at experimental embryology. He "exposed the little animal [the chick embryo] by putting it into water heated to about 104° F. just covering the egg" and "hoped to keep it alive by these means and observe in the same chick the whole progress of growth, but it soon died"; therefore, he says "I was obliged to have recourse to a succession."[30] He was an experimental surgeon, as may be shown from the following quotation[31] from one of his lectures:

"Here is the testicle of a cock, separated from that animal and put through a wound, made for that purpose, into the belly of a hen, which mode of turning hens into cocks is much such an improvement for its utility as that of Dean Swift when he proposed to obtain a breed of sheep without wool. The hen was afterwards killed and the testicle was found adhering to the intestines, as may be seen in this preparation where the parts are preserved."

He devised and carried out experiments to ascertain whether the growth in a cock's spur is due to a "disposition" inherent in the spur or derived from the constitution of the cock. He excised spurs from the legs of cocks and implanted them in their combs to note the rate of growth under such unfamiliar surroundings. The first vital stain ever used was madder; it was introduced to the notice of biologists in 1764 by John Belchier, surgeon to Guy's Hospital; by its experimental application John Hunter revolutionized our knowledge of bone growth and bone decay.[32] In the hands of Professor A. V. Hill the measurement of heat in living tissue has become the most delicate and certain indication of the nature of their vital reactions. The manner in which living matter reacted to

the application of heat and cold, and to a degree of heat generated in living tissues, Hunter made the subject of an endless number of investigations, all with the practical view of ascertaining how much or how little should be done to keep damaged human tissues alive.[33] Here was, as we have seen, an experimental physiologist and also an experimental pharmacologist.[34] He was a psycho-analyst;[35] he tried to inoculate an ass and a bitch with the virus of syphilis.[36] He preached the doctrine of operating at the earliest possible stage of a disease, and, placing himself in the position of the patient, said, "Nor do I go further than I now think I would have performed on myself were I in the same situation."[37] He performed experiments on the sensitive plant which are now being repeated.[38] These are only some of the points in which Hunter has anticipated modern progress.

So much for the past in its relation to our greatest men. What of the future?

The Future.

As I look forward I like to humour my fancy and indulge my dreams. Imagination, Keats tells us, may be compared to Adam's dream—he awoke to find it truth. The art of the surgeon is the pillar of science, and it is for science to discover how that almost perfect art may now be used to the fullest advantage. We eagerly await the day when disease shall not require to be checked in high career, but shall be blighted at its origin, or even denied existence, when our weapons of war shall be laid aside. That day may yet be far away, but already beyond the distant hills we see promise of the dawn. It does not, perhaps, so much or so deeply concern ourselves as those who soon must take up our task, and lead the hosts whose victory shall attain our high ideal. In due time, and in accord with ancient precedent, this country of ours, the fruitful mother of so many gifted sons, shall raise up in our schools the youths who shall go forth to conquer a crown. They will be best equipped who keep to the course, recall the methods, and are imbued with the ardent spirit of the two famous men whom we praise to-day—the two greatest surgeons the world has ever known.

Our youths must be prepared for self-sacrifice, for arduous discipline, perhaps for the most heart-breaking rebuffs, for the stern or even bitter criticism of their fellows. But there never was a time so rich in promise, so laden with rewards for those who labour with sincerity and truth. They will not travel alone. The whole army of science is in league with them, moving forward with incredible speed, eager to lay at their feet the triumphs of its astounding conquests. The responsibilities which rest on them, the intellectual accomplishments and the dedication of their lives demanded of them, are enough to cause the stoutest heart sometimes to falter. Yet, armed with the sword of the spirit and the breastplate of faith, they will remember that the happiness of life lies in its responsibilities, that true joy is found in the search for what may after a weary journey prove unattainable. Ahead lies the noblest of tasks to which they may consecrate themselves: for the lives of men are in their hands, the love, the happiness, the whole welfare of mankind. We need not fear. They will be worthy of their charge. God counts not result but effort.

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EXPERIMENTAL PRODUCTION OF ACUTE AND CHRONIC ARTHRITIS AND ARTICULAR NEOPLASM BY RADIUM.*

(With Special Plate.)

BY

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A FEW years ago, in a Hunterian Lecture on osteo-arthritis, I ventured the opinion that the peculiar proliferations of bone and cartilage often occurring in the more chronic form of arthritis usually known as osteo-arthritis, some of which attain a very considerable size, were intermediate between a frankly inflammatory process and a genuine neoplasm. The difficulty experienced in distinguishing between the two was so great that some of the loose bodies occurring in osteo-arthritis were designated "synovial chondromata" by Professor Shattock and myself. It is unnecessary to enter now into the histological differences between such forms of proliferation and frankly inflammatory developments. It is interesting to note, however, that the form of chronic arthritis usually known as "rheumatoid arthritis" or "chronic arthritis of the synovial or mixed types" (Fisher) is a frankly inflammatory process, whereas the proliferative changes in the so-called "osteo-arthritis" belong to the peculiar type of proliferation akin to new growth that we are considering. It is interesting to note also that the age incidence of osteo-arthritis or chronic arthritis of the chondro-osseous type is, as a general rule, very similar to that of many forms of malignant change, particularly the carcinomatous—that is, they both occur when the resistance of the body to irritation of *moderate* degree of intensity is beginning to diminish because the patient has passed the meridian of life. In younger organisms the vascular response to irritation of slight or moderate intensity is marked, and, combined with a moderate degree of cellular proliferation, probably suffices to cope with minor degrees of irritation.

After the meridian of life is past the vascular reaction is not so much in evidence, and a slight but persistent form of irritation tends to bring about a proliferation of cells that are fairly well nourished but degeneration of cells whose nourishment is poor. A good example of this is seen in "osteo-arthritis." The physiological basis for the changes in the latter is that while the central part of the articular cartilage which is devoid of blood vessels is poorly nourished, the extreme lateral portions receive blood vessels from the circulus articuli vasculosus. Irritation, therefore, whether mechanical or toxic, tends to cause degeneration of the central portion of the articular area and proliferation of the lateral portions. We observe this same peculiar admixture of proliferation and degeneration in many forms of true neoplasm, both innocent and malignant. It appears that in new growths we are faced with an essential alteration. There is a breaking down of the physiological harmony between cells and the inhibiting intercellular substance. We can imagine, for example, that prolonged irritation or toxaemia might have, simultaneously, a stimulating effect upon cells but an inhibiting effect upon intercellular substance. On the other hand, inhibition might be at a very low ebb from the degeneration of old age, and might, in a person with suitable disposition, cause a growth to develop. If inhibition is temporarily abolished but eventually recovers, a so-called innocent new growth may result, which after a time ceases to develop actively. If inhibition is impaired a subinflammatory process such as osteo-arthritis develops (compare prostatic adenomata). If it is severely impaired and the irritation is moderate, or if it is slightly impaired and the irritation great, or if irritation is great and inhibition severely impaired, a malignant growth results.

As according to this theory the condition known as "osteo-arthritis" is a stage intermediate between inflammation and new growth, it seemed to me that it might be of considerable interest to ascertain whether it would be

* The expenses of this research were defrayed by the Medical Research Council.

possible to bring about osteo-arthritis and new growth experimentally through the same agency, and for this object tubes containing radium were introduced into the knee-joints of rabbits. The following experiments show the results obtained.

A. *Experiments with Radium contained in Glass Tubes.*

Fig. 1 represents the left knee-joint of a full-grown rabbit, and shows well marked proliferation of the cartilage of the inner and upper margin of the trochlear surface of the femur.

Experiment 20 (*Old Series*).—The left knee-joint of a rabbit was opened by an incision upon the internal aspect and under strict aseptic precautions. A glass tube containing 0.0382 mg. of radium bromide was fixed by a catgut suture against the inner margin of the trochlear surface, and the joint carefully closed by suture. The joint was immobilized as far as possible by several layers of gauze saturated with collodion. A glass tube containing 0.15 mg. radium bromide was fixed in a similar position in the right knee-joint. The rabbit remained perfectly healthy, and nineteen weeks later was killed. The left knee-joint revealed the presence of a large chondro-osteophyte similar to those seen in osteo-arthritis (Fig. 1). It had developed from that portion of the articular edge opposite to where lay the radium tube, which had formed for itself an oblong shallow pit in the adjacent part of the internal femoral condyle. The remainder of the joint showed no obvious change beyond localized synovial hypertrophy in the vicinity of the radium tube. The right knee-joint showed similar changes, but to a lesser degree.

Experiment 19 (*Old Series*).—The left knee-joint of a rabbit was opened as above, and a glass tube containing 0.15 mg. of radium bromide was fixed against the inner border of the internal condyle of the femur. The animal was killed four weeks later, and it was noted that well marked proliferation of the lateral part of the cartilage had occurred at the junction of the internal condyle with the trochlear surface of the femur. A patch of fibrillation of the cartilage had occurred more centrally. Localized synovial hypertrophy was again present.

Experiment 6 (*New Series*).—A glass tube containing 0.15 mg. of radium bromide was introduced into a similar position in the right knee-joint of a rabbit. Two weeks later the animal died, and it was noted that no alteration in bone and cartilage had occurred, but that a localized villous synovitis was present in the immediate vicinity of the tube.

Experiment 5 (*Old Series*).—A glass tube containing 0.15 mg. of radium bromide was introduced into the suprapatellar pouch of the right knee-joint of a rabbit. Fourteen months later the animal was killed. The radium tube had created for itself a deep pit above the trochlear surface. Slight osteo-arthritic changes were present. An interesting feature was the fact that the patella had become dislocated, and lay upon the outer side of the femoral condyle. Here an articular surface had developed for the patella with a covering of newly formed articular cartilage (Fig. 4).

B. *Experiments with Radium contained in Platinum Tubes.*

Experiment 2 (*New Series*).—The left knee-joint of a rabbit was opened from the inner side under scrupulous aseptic technique, and three platinum tubes containing radium were introduced as follows:

Platinum tube No. 151, containing 1.2 mg., into the outer part of the suprapatellar pouch.
Platinum tube No. 152, containing 0.50 mg., into the inner part of the suprapatellar pouch.
Platinum tube No. 153, containing 0.51 mg., into the lower and anterior part of the joint. Total 2.21 mg.

After an interval of several weeks the animal developed acute destructive suppurative arthritis of a fulminating type, which necessitated its destruction. It is highly improbable that the infection was introduced at the time of the operation owing to the interval that elapsed.

Experiment 1 (*New Series*).—The left knee-joint of a rabbit was opened from the inner aspect, and platinum tube No. 150, containing 2.44 mg. of radium, was introduced into the joint. The animal was killed eleven months later, and the following conditions were observed (Fig. 2). A condition of chronic arthritis of mixed type or "rheumatoid arthritis" had developed. The radium tube lay in front of the crucial ligaments. The articular ends of both tibia and femur were considerably enlarged from inflammatory thickening of the periosteum. Considerable destruction of the articular surfaces of both femur and tibia had occurred, associated with the formation of chondro-osteophytes at the articular margins. This formation of new bone was particularly well marked from the antero-internal part of the internal tibial condyle, where a very large osteophyte had developed (see drawing). Adhesive ankylosis occurred in places between the adjacent surfaces of the femur and tibia. The synovial membrane was inflamed, and in places invaded the articular surface in the form of pannus.

Experiment 4 (*New Series*).—The left knee-joint of a rabbit was opened from the inner side. Two platinum tubes, one containing 0.22 mg. and the second 0.24 mg. of radium bromide, were introduced into the joint cavity (suprapatellar pouch). The animal was killed fourteen months later, and the following interesting conditions were observed (Fig. 3).

The joint was enormously enlarged, partly from a fluid swelling occupying the inner part of the joint and partly from a hard tumour-like mass growing from the lower end of the femur and projecting backwards into the popliteal space, but also inwards. On carefully opening the joint it was seen that the fluid swelling on the inner side was an abscess cavity, containing thick, curdy, purulent fluid, and in which the radium tubes lay. Internally the cavity had a dense fibrous wall, whereas externally the wall of the abscess cavity was formed by the enlarged lower end of the femur. In sagittal section the shape, size, and general relations of the tumour are demonstrated clearly. It is seen to be developing principally from the inner and posterior aspects of the lower end of the femur; to be of a somewhat dense and compact consistency, and to be covered externally by a tough periosteal envelope. Histologically the tumour is clearly an ossifying periosteal sarcoma which has originated from the periosteum covering the intra-articular portion of the diaphysis and the adjacent portion of the epiphysis of the internal femoral condyle.

I am indebted to Professor H. M. Turnbull, Director of the Pathological Institute, London Hospital, for the following report upon the tumour:

The peripheral portions of the mass for a considerable depth consist of a very cellular tissue that is invading and destroying muscle. The cells are spindle-shaped, triangular, polygonal, and spherical, vary greatly in size, but are for the most part large. Deeper in the mass very numerous swollen collagenous fibres appear among the cells, and gradually enlarge to form a close irregular meshwork of very narrow osteoid trabeculae. As still deeper layers are followed the trabeculae become gradually stouter, and enclose larger medullary spaces, in which lie essentially similar, usually degenerated, cells; these trabeculae are of coarse-fibred bone, are for the most part necrosed, and are arranged very irregularly. In the section from the maximal convexity of the mass some large medullated nerves are included in this tissue, and the adventitia of an artery is replaced by the polymorphic cells. The femur as it touches the mass is cut tangentially; the mass replaces the periosteum, but the corticalis is neither necrosed nor interrupted. The medulla of this portion of femur is, however, filled with a close meshwork of trabeculae of necrosed coarse-fibred bone, with some superimposed finely fibrillated bone or osteoid tissue; the medullary spaces contain the polymorphic cells, and these cells show extensive degeneration and necrosis. Similar cells fill some of the inner Haversian spaces and canals of the corticalis.

There are a considerable number of leucocytes within the mass and in places close to it; there are leucocytic thrombi in some large vessels near the mass, and there is much perivascular infiltration with plasma cells in the muscle at a distance from the mass.

The conditions to be separated for a diagnosis are: (1) inflammation leading to bone formation, (2) callus formation following trauma, and (3) neoplasm. The features which I have tried to sketch in the description, particularly the wide peripheral zone of destructive cellular infiltration, make, I think, the diagnosis of osteo-sarcoma undoubted. There is some inflammatory infiltration in the mass and in the tissue beyond the mass, but this infiltration is relatively insignificant, and is such as is frequently found in association with malignant neoplasms. The sections alone do not suffice to settle the origin of the growth, but, taken in conjunction with your pictures, there can be little doubt that the sarcoma arose in the periosteum of the femur, and had invaded the medulla nearer the centre of the mass than the site of the section that includes femur.

I conclude that the condition is an osteo-sarcoma of the periosteum of the lower end of the femur.

It is not claimed that these experiments are anything more than suggestive, and it is obvious that confirmatory evidence will be necessary. The first fact that demands our notice is that, in the series of experiments with small quantities of radium contained in glass tubes, the reaction of the joint elements was slight or moderate and took the form of proliferation of the better nourished edges of the articular cartilage or synovial hypertrophy in the vicinity of the tube. The experiments were conducted under rigid aseptic technique, and suppuration did not occur. The localized proliferations at the edges of the articular